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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,920	03/22/2001	Sherman Fong	P1192-2	6172

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/816,920	FONG ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *08 December 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☐ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *15-17,19,20,27-31 and 47*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

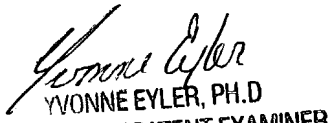
10.☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: claims 15-17, 19, 20, 27-31 and 47 stand rejected under 35 USC 101 because the claimed invention is not supported by a substantial utility. The basis for this rejection is set forth at pages 2-4 of the previous Office Action (16 October 2003). Applicants state that the legal standard accepts that in vitro or animal model data is acceptable utility as long as the data is "reasonably correlated" to the pharmaceutically utility. Applicants assert that the mixed lymphocyte reaction (MLR) is a well established in vitro assay for assessing the ability of a test compound to stimulate T cell proliferation. Applicants state that MLR has been extensively used and is considered to the best in vitro model available to study graft-versus host disease and graft rejection and identify immunostimulators. Applicants state that the Bolekine protein stimulates proliferation over control; by 112% an 192.7% for the respective concentrations and that a sequence analysis of the Bolekine protein determines that Bolekine is a member of the CXC family of chemokines. Applicants maintain that chemokines are known in the literature for stimulating leukocyte movement, stimulating proliferation and activation of different immune cells.

Applicants state that the Examiner has rejected the claims solely on the alleged basis that the in vitro MLR assay is an in vitro assay and not predictive of the immune response in general. Applicants submit that the MLR assay is used to examine only immune cell proliferation and this is reflected in the claims. Applicants argue that the Examiner has not taken into consideration that the Skin Vascular Permeability assay is an in vivo assay, demonstrating another trait of the chemokine family, that of chemotaxis. Inflammatory cells migrat to the site of injection. Applicants argue that based on the in vitro MLR assay, the in vivo Skin Vascular Permeability Assay and the structure of Bolekine as a CXC chemokine, there is proof that Bolekine is a chemoattractant and stimulator of immune cells, consistent with the characteristics of the chemokine family. Applicants submit that the in vitro and animal model data provided within the specification is reasonably correlated utility within the scope of claims as defined by the legal standard.

Applicants arguments have been fully considered but not found persuasive. Applicants have stated that MLR has been used to study graft-versus-host disease, identify immunostimulators and have cited diverse diseases/conditions such as cancer, compromised immune systems, psoriasis, hepatitis, renal disease, arthritis.The ability of the Bolekine protein to stimulate T cell proliferation in the MLR assay does not provide for what specific conditions or for what specific diseases the claimed invention would predictably function. Furthermore, as was stated in the last Office acton, the reaction caused by the Bolekine protein in the MLR assay is not predictive of general responses of the immune system because activation of a lymphocyte is controlled not only by antigen binding but also by interactions with other cells Thus, the Examiner has not rejected the claims solely on the basis of an in vitro assay. The Examiner has rejected the claims because the MLR assay is not the correct model. Applicants cite the Skin Vascular Permeability assay (an in vivo assay) as demonstrating the migration of inflammatory cells in the presence of Bolekine, but fail to disclose which disease condition this mechanism would be beneficial.

The results of the MLR assay do not support a specific and substantial utility for the claimed invention because this particular assay is not predictive of immune response in general, and one of ordinary skill in the art would not expect a stimulatory effect in the MLR assay to correlate to a general stimulatory effect on the immune system, absent evidence to the contrary. The scientific reasoning and evidence a a whole indicates that the rejection should be maintained.



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